



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : A61K 7/48, 7/15, 7/155, 7/50	A1	(11) International Publication Number: WO 98/13021 (43) International Publication Date: 2 April 1998 (02.04.98)
(21) International Application Number: PCT/FI97/00577 (22) International Filing Date: 25 September 1997 (25.09.97) (30) Priority Data: 963849 26 September 1996 (26.09.96) FI (71) Applicant (for all designated States except US): CULTOR LTD. [FI/FI]; Kyllikinportti 2, FIN-00240 Helsinki (FI). (72) Inventor; and (75) Inventor/Applicant (for US only): JUTILA, Kirsti [FI/FI]; Rantapolku 2 B 10, FIN-02170 Espoo (FI). (74) Agent: KOLSTER OY AB; Iso Roobertinkatu 23, P.O. Box 148, FIN-00121 Helsinki (FI).		(81) Designated States: DE, GB, JP, US, European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published <i>With international search report.</i>
(54) Title: PREPARATION PROTECTING SKIN FROM MECHANICAL IRRITATION (57) Abstract <p>The invention relates to cosmetic preparations, particularly skin care products, shaving preparations, and depilatory preparations, which protect skin from mechanical irritation. The active agent contained in the preparations is trimethylglycine. The invention also relates to the use of trimethylglycine as a skin-protecting agent in different cosmetic preparations, and to a method of protecting skin from mechanical irritation.</p>		

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NI	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakhstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	IJ	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

PREPARATION PROTECTING SKIN FROM MECHANICAL IRRITATION

FIELD OF INVENTION

The present invention relates to cosmetic preparations, particularly to skin care products, shaving preparations, and depilatory preparations ('lady shaving' preparations), which protect skin from mechanical irritation. The active agent contained in the preparations is trimethylglycine. The invention also relates to the use of trimethylglycine as a skin-protecting agent in different cosmetic preparations, and to a method of protecting skin from mechanical irritation.

10 BACKGROUND OF INVENTION

Skin is subjected to mechanical irritation, i.e. it is scratched, abraded, chafed or cut, in many situations. When men shave, a razor or the blade of a shaver may scratch or cut the skin on the face despite the use of shaving lather or shaving soap. Women, in turn, cut hair off the legs, armpits, and groin, where the skin is extra sensitive, and the treatment easily scrapes or cuts the skin. Infants and persons using incontinence diapers have the problem that their skin often moistens and thereby becomes thinner, and the diaper chafes and damages the skin. Shoes, in turn, abrade the skin on the heels, ball of the foot, and toes, and the skin on the hands is easily abraded and scratched in agricultural and garden work.

Cut, sore skin aches, smarts, and feels tight; microwounds are subjected to inflammation; and application of common cosmetic preparations to the skin does not necessarily ease the discomfort, nor protect the skin. On the contrary, application of a preparation on cut, sore skin often adds to smarting and skin irritation.

The object of the present invention is to provide a preparation protecting skin from mechanical irritation.

Another object of the present invention is to provide a method of protecting skin from mechanical irritation.

30 BRIEF DESCRIPTION OF INVENTION

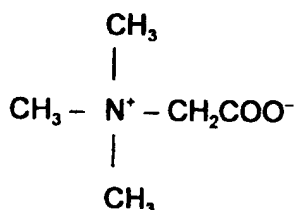
Surprisingly, it has been discovered that trimethylglycine protects skin from cutting, scratching, abrasion, chafing, and other mechanical irritation, and so trimethylglycine can be used in different cosmetic preparations as an agent protecting skin from such irritation. The present invention thus relates to

the use of trimethylglycine as an agent protecting skin from mechanical irritation in cosmetic preparations, particularly in skin care products, shaving preparations, and depilatory preparations. The present invention also relates to a cosmetic preparation that contains trimethylglycine as an ingredient
 5 protecting skin from mechanical irritation. The present invention further relates to a method of protecting skin from mechanical irritation by applying a trimethylglycine containing cosmetic preparation to the skin.

DETAILED DESCRIPTION OF INVENTION

In the present invention, mechanical irritation means external
 10 damage caused to epidermis by different objects, such as a shaver blade, a razor, shoes, a diaper, clothes, tools, or the like. A cosmetic preparation here means different skin care products, such as skin creams, cleansers, tonics, and milks; hand creams; foot care products, such as foot creams, and foot baths; shaving preparations, such as after-shave lotions, shaving lathers,
 15 foams, gels, and balms; depilatory preparations; products of personal hygiene ('lady-shaving' preparations), and the like. Preferred preparations according to the invention are foot care products, after-shave lotions, skin tonics, and baby care products.

In the present invention trimethylglycine means a naturally occurring
 20 quaternary ammonium type compound having the formula



25 which is present as an anhydride or a monohydrate. The compound is commonly also called betaine, trimethylammonioacetate, 1-carboxy-N,N,N-trimethylmethanaminium, inner salt, and glycine betaine. In the pure form, it is a white, crystalline compound that is readily soluble in water, and in lower
 30 alcohols, such as methanol and ethanol. In plants it functions as an osmolyte and thereby protects cells from the effects of osmotic stress.

Trimethylglycine has a bipolar structure, and it contains several metabolically reactive methyl groups, which it can donate in enzyme catalyzed reactions. Most organisms are able to synthesize small amounts of
 35 trimethylglycine, e.g. for the methyl donor function, but are not able to produce it, nor store it, in large amounts.

At cell level, trimethylglycine has been observed to protect plants particularly under stress conditions. It has been used as an agent improving the preservation characteristics of a plant, and as an agent improving the drought and chill resistance of a growing plant. To enhance growth, trimethylglycine has also been added to fertilizers. Further, trimethylglycine has been used as an additive in animal feed or fodder. It has also been observed to have pharmacological activity, e.g. it prevents detrimental effects of coccidiosis in broilers.

Synthetic long-chain alkyl ester, sulpho, and aluminium salt derivatives of trimethylglycine, commonly - and slightly misleadingly - called 'betaine derivatives' or 'betaines', have long been used as amphoteric surfactants in cosmetic industry, that is, e.g. as foaming agents in shampoos, soaps, and cleansers. As examples are mentioned U.S. Patents 4,490,355 and 4,654,161. Trimethylglycine, instead, is not useful in the above-mentioned cosmetic applications, since its surface activity is completely different, and since it does not foam at all.

The surprising effect of trimethylglycine presented in the invention, i.e. that it protects skin from mechanical irritation, has not been described earlier, although trimethylglycine has been used for other purposes in cosmetic industry. EP 531,387 teaches that a preparation containing trimethylglycine reduces irritation caused by skin-irritating ingredients of a cosmetic preparation, such as cationic compounds, quaternary ammonium compounds, solvents, surfactants, and aseptic agents. EP 56,595 teaches a hair conditioning composition that contains 0.1 to 25% by weight of betaine, and 0.1 to 10% by weight of aliphatic organic acid, such as citric acid, and is stated to act as a hair conditioner, an antioxidant, and a buffer. German Patent 1,911,144 teaches a skin care composition that contains urea and lactic acid, and a cream base that can contain amino acid derivatives, such as betaine.

Trimethylglycine hydrochloride - since it is strongly acidic - differs in its characteristics from trimethylglycine anhydride and trimethylglycine monohydrate, has also been used in cosmetic products. Hungarian Patent T50,622 teaches a skin care composition that contains e.g. 0.3 to 0.6% of betaine hydrochloride.

EP 2,127 describes a shaving composition containing 'cosmetically acceptable betaine', which means particularly long-chain alkyl esters of glycine, the composition being stated to affect the root of a hair, so that the

hair can be cut as close to the skin as possible, which improves the shaving result.

The best known organisms producing large amounts of trimethylglycine are plants of the genus *Chenopodiaceae*, such as sugar beet, and some microbes and marine invertebrates. It can be obtained e.g. from sugar beet by chromatographic methods. Trimethylglycine is commercially available both as an anhydride and as a monohydrate from Cultor Oy, Finnsugar Bioproducts.

A cosmetic preparation according to the present invention protecting skin from mechanical irritation contains 0.1 to 20% by weight, preferably 2 to 10% by weight, particularly 2 to 6% by weight of trimethylglycine as an anhydride or as a monohydrate in an aqueous composition or cream base, which may be e.g. an oil-in-water or a water-in-oil emulsion, water, or a water/alcohol mixture. The preparation also contains ingredients and additives that are commonly used in the cosmetic preparation concerned. They may be, for example, skin care agents, softening agents, astringent agents, refreshing agents, anti-oxidation agents, emulsifying agents, viscosity increasing agents, moisturizing agents, stabilizing agents, colouring agents, perfumes, surfactants, and the like, as well as alcohols and/or water.

The cosmetic preparations according to the invention include, in particular, skin care products, shaving preparations, depilatory preparations, and products of personal hygiene, such as skin tonics and milks; skin creams and lotions; cleansing creams, milks and gels; liquid cleansers; foot creams and baths; hand creams; refresher and moisturizing tissues and sprays; after-shave lotions; shaving lathers, gels and balms; and foam preparations. The preparation type is selected according to the need. The preparations of the invention can be formulated by common methods well known to those skilled in the art.

The use of trimethylglycine in the above preparations provides the products with characteristics that protect skin from mechanical irritation. As trimethylglycine also reduces the effect of any irritating agents contained in the cosmetic preparation, as described in EP 531,387, preparations containing trimethylglycine can be regarded as being particularly friendly to the skin.

It has been observed that trimethylglycine protects skin from mechanical irritation particularly effectively when it is applied as close as

5.

possible to the moment when the epidermis is cut, i.e. almost at the very moment that the damage is done. In the method of the invention for protecting skin from mechanical irritation, a preparation according to the invention can thus be applied to the skin at the very moment that the skin is subjected to irritation, or even before it. For example, when one wants to protect the skin from being cut and scratched by the blade of a shaver during shaving or cutting off of hairs, a preferred preparation according to the invention might be a shaving lather or foam, to ensure that skin-protecting trimethylglycine is immediately present on the skin. If the preparation according to the invention is an after-shave lotion or a skin tonic, it will be applied to the skin immediately after shaving or cutting off of hairs. When one wants to protect the skin from being chafed by a diaper, a cream according to the invention can be applied to the skin before putting on a new diaper, or the skin can be washed or wiped with a cleanser or a moisturizing tissue according to the invention. Foot or hand creams according to the invention can be used according to the need for symptomatic alleviation of irritation, or for preventing irritation.

The invention will be described in greater detail by means of the following examples. The examples are only intended to illustrate the invention, and they are not to be regarded as restricting the scope of the invention in any way.

EXAMPLE 1

EFFECT OF TRIMETHYLGLYCINE ON SKIN IRRITATION

The effect of trimethylglycine on the skin was studied by measuring the thermal conductivity of the skin by a method described by A. Dittmar in *Cutaneous investigation in health and disease. Non-invasive methods and instrumentation*, ed. J.L. Lévêque, Marcel Dekker Inc., New York-Basel, 1989. The method correlates directly with microcirculation on the skin. Thermal conductivity (K) is measured from the skin with a specific Hematron® thermal sensor and transformed into an electric signal, which is recorded by a recorder. In thermal conductivity (ΔK), a significant level of variation is 0.1 mW/cm · °C.

The test was conducted on two test groups, each one of which comprised six healthy female volunteers. In the first test group (group 1), four cutaneous test areas were defined on the arm of each subject, and microcirculation was first measured for 30 minutes before the preparation was

added. The skin was then cut by scraping in all the four areas, and onto the skin was pressed a filter paper into which a solution had been absorbed that contained $14 \mu\text{l}/\text{cm}^2$ of 4% (weight/volume) trimethylglycine in distilled water, or only distilled water (placebo). Subsequently, microcirculation was measured for 60 minutes at the erythematous, damaged points on the skin, treated with the solution.

In the second test group (group 2), the subjects' microcirculation was measured at the erythema in the same way as above, but the irritation was here caused by 30-minute infrared irradiation (IR Philips 250 S lamps, spectrum 700 to 2500 nm, power 250 W, light energy $70 \text{ mW}/\text{cm}^2$, irradiation area 14 cm^2) in the four cutaneous areas defined on the upper back.

The thermal conductivity values measured on each volunteer subject are shown in table 1 (group 1) and table 2 (group 2). Tables 1 and 2 show the mean values ($n=6$) of thermal conductivity (K expressed as $\text{mW}/\text{cm} \cdot ^\circ\text{C}$) in the treated area, placebo area, and untreated areas at different instances of measuring. In tables 1 and 2, the treated area means an area treated with a preparation containing trimethylglycine; untreated area 1 is an untreated area that is symmetric with the area treated with the preparation containing trimethylglycine; the placebo area means an area treated with a placebo; and untreated area 2 is an untreated area that is symmetric with the area treated with the placebo.

Table 1

Mean values of thermal conductivity (K), expressed as $\text{mW}/\text{cm} \cdot ^\circ\text{C}$, in mechanical skin irritation

	time t_0^1	t_{30}^2	t_{60}^3
treated area	3.82 ± 0.59	3.66 ± 0.69	3.42 ± 0.41
untreated area 1	3.57 ± 0.27	3.77 ± 0.22	3.91 ± 0.29
placebo area	3.94 ± 0.48	3.82 ± 0.23	3.81 ± 0.18
untreated area 1	3.28 ± 0.28	3.36 ± 0.34	3.50 ± 0.23

Table 2

Mean values of thermal conductivity (K), expressed as mW/cm · °C, in thermal skin irritation

	time t0 ¹	t30 ²	t60 ³
treated area	3.13 ± 0.30	3.85 ± 0.31	3.60 ± 0.38
untreated area 1	3.61 ± 0.25	3.68 ± 0.22	3.84 ± 0.26
placebo area	3.45 ± 0.21	3.74 ± 0.27	3.26 ± 0.20
untreated area 2	3.72 ± 0.29	3.46 ± 0.32	3.58 ± 0.36

¹ before application of product

5 ² 30 min after application of product

³ 60 min after application of product

treated area = area treated with product

10 Per cent (%) variations between the treated area and untreated area 1, and the placebo area and untreated area 2 were calculated for each volunteer subject 30 and 60 min after application of the product. The variations were calculated using the formula

$$\% \text{ var} = \frac{(TZ_i - TZ_0) - (NTZ_i - NTZ_0)}{TZ_0 + (NTZ_i - NTZ_0)} \cdot 100$$

15 where

TZ_i = treated area or placebo area at time instant t30 or t60

TZ_0 = treated area or placebo area at time instant t0

NTZ_i = untreated area 1 or untreated area 2 at time instant t30 or t60

20 NTZ_0 = untreated area 1 or untreated area 2 at time instant t0.

The mean values of the per cent variations and the standard errors of the mean values (n=6) in group 1 and group 2 are shown in tables 3 and 4, respectively.

Table 3

25

% Variation, group 1

	t30 min	t60 min
treated area / untreated area 1	-8.9 ± 8.6	-15.0 ± 8.8
placebo area / untreated area 2	-0.8 ± 8.9	-4.6 ± 8.2

When a preparation containing trimethylglycine, diluted at a concentration of 4% (weight/volume) in distilled water, was applied to the skin, microcirculation reduced (mean variation: $-8.9 \pm 8.6\%$) after 30 min. An even more significant reduction in the microcirculation was achieved after 60 minutes of treatment (mean variation: $-15.0 \pm 8.8\%$).

In the placebo area, the microcirculation does not vary 30 and 60 min after treatment.

Table 4
% Variation, group 2

	t30 min	t60 min
treated area / untreated area 1	23.5 ± 11.8	10.8 ± 14.5
treated area / untreated area 2	19.7 ± 8.2	-0.6 ± 6.7

10

When a preparation containing trimethylglycine, diluted at a concentration of 4% (weight/volume) in distilled water, was applied to the skin, microcirculation increased (mean variation: $23.5 \pm 11.8\%$) after 30 min. No variation was observed in the microcirculation 60 min after the treatment (mean variation: $+10.8 \pm 14.5\%$).

15

In the placebo area, microcirculation increased 30 min after the treatment (mean variation: $+19.7 \pm 8.2$), but 60 min after the treatment, no variation was observed in the microcirculation (mean variation: -0.6 ± 6.7).

As compared with the placebo, a preparation containing trimethylglycine diluted at a concentration of 4% (weight/volume) in water was effective against mechanical erythema (group 1) after normal application. The effect was detected 60 min after the application. The results show that the preparation is effective against skin irritation when the damage is relatively superficial. In addition, cutting of the skin causes erythema and probably enhances penetration of the preparation, which in turn adds to the effect of the preparation.

20

25

Instead, a preparation containing trimethylglycine had no effect on thermal erythema (group 2). No problems arose in respect of sensitivity in either of the tests: the subjects tolerated the trimethylglycine preparation well.

30

Figs. 1A (group 1) and 1B (group 2) are diagrams drawn on the basis of the results.

EXAMPLE 2

This example describes different preparations according to the present invention.

	Baby lotion 1	
5	Mineral oil	26.00%
	Lanolin	1.04%
	Stearic acid	0.94%
	Triethanolamine	0.52%
	Water	65.68%
10	Trimethylglycine	4.00%
	Stearyl alcohol	0.94%
	Cetyl alcohol	0.52%
	Sodium alginate	0.36%
	Perfume	q.s.
15	Baby lotion 2	
	Cetyl stearyl alcohol	1.00%
	Mineral oil	4.00%
	Polysorbate 60	1.70%
	Sorbitan isostearate	1.00%
20	Glyceryl stearate	1.00%
	Liquid lanolin	0.25%
	Water	81.35%
	Trimethylglycine	4.00%
	Hydroxyethyl cellulose	0.20%
25	Glycerine	5.50%
	Perfume, preservative	q.s.
	Foot cream 1	
	Glyceryl monostearate	15.00%
	Lanolin	1.00%
30	Sorbitol syrup, 70%	2.50%
	Glycerine	2.50%
	Antimicrobial agent	0.25-0.50%
	Trimethylglycine	4.00%
	Water	balance 100.00%
35	Foot cream 2	
	Glyceryl monostearate	12.0%

10

	Mineral oil	2.0%
	Glycerine	3.0%
	Spermaceti substitute	5.0%
	Camphor	1.0%
5	Methyl salicylate	1.0%
	Water	69.9%
	Trimethylglycine	6.0%
	Preservative	0.1%
	Foot cream 3	
10	Ottasept extra	1.00%
	Lexemul AR	16.00%
	Cetyl alcohol	1.00%
	Amerchol L-101	3.00%
	Solulan 98	0.50%
15	Mineral oil	3.00%
	Alcloxa	0.25%
	Propylene glycol	5.00%
	Distilled water	65.95%
	Trimethylglycine	4.00%
20	Perfume	0.3%
	Bay salt foot bath	
	Potassium iodide	1 part
	Potassium bromide	2 parts
	Magnesium chloride	250 parts
25	Calcium chloride	125 parts
	Magnesium sulphate	250 parts
	Sodium sulphate	500 parts
	Sodium chloride	1500 parts
	Trimethylglycine	500 parts
30	Colouring agent, perfume	q.s.
	Foot bath	
	Cocamidopropylbetaine	45%
	Aminoxid WS35	3%
	Cocamidopropylaminoxide	3%
35	TEGO 103S	5%
	Undecylene diethanolamide	2%

11

	Lactic acid	5%
	Trimethylglycine	10%
	Water	30%
	Perfume	q.s.
5	After-shave lotion	
	Ethyl alcohol, denatured	56%
	Propylene glycol	3%
	Trimethylglycine	4%
	Water	36%
10	Perfume	1%
	Astringent after-shave gel	
	Dipotassium glycyrrhizinate	1.0%
	Citric acid	0.5%
	Zinc sulphate	0.2%
15	Zinc phenol sulphonate	0.2%
	Ethyl alcohol	10.0%
	Propylene glycol	5.0%
	Trimethylglycine	2.0%
	Water	81.8%
20	Perfume, preservative	q.s.
	Soap-free after-shave cream	
	Glyceryl monostearate S/E	10.0%
	Mineral oil	10.0%
	Vaseline	6.0%
25	Tegiloxan 100	0.5%
	Lanolin	3.0%
	Cetyl alcohol	3.0%
	Glycerol	3.0%
	Citric acid	0.2%
30	Potassium aluminium sulphate	0.1%
	Trimethylglycine	4.0%
	Water	60.2%
	Perfume	q.s.

CLAIMS

1. Use of trimethylglycine as an anhydride or a monohydrate in cosmetic preparations for protecting skin from mechanical irritation.
2. Use according to claim 1, **characterized** in that trimethylglycine is used in a concentration of 0.1 to 20% by weight, preferably 2 to 10% by weight, particularly 2 to 6% by weight, based on the preparation.
3. Use according to claim 1 or 2, **characterized** in that the cosmetic preparation is a skin care product, a shaving preparation or a depilatory preparation.
4. Use according to any one of claims 1 to 3, **characterized** in that the cosmetic preparation is a foot care product or a hand cream.
5. Use according to any one of claims 1 to 3, **characterized** in that the cosmetic preparation is a baby care product.
6. Use according to any one of claims 1 to 3, **characterized** in that the cosmetic preparation is an after-shave lotion or a skin tonic.
7. A cosmetic preparation protecting skin from mechanical irritation, **characterized** by containing trimethylglycine as an anhydride or a monohydrate in a concentration of 0.1 to 20% by weight, preferably 2 to 10% by weight, particularly 2 to 6% by weight, based on the preparation, in a suitable conventional cosmetic base.
8. A preparation according to claim 7, **characterized** in that the preparation is a skin care product, a shaving preparation or a depilatory preparation.
9. A preparation according to claim 7 or 8, **characterized** in that the preparation is a foot care product or a hand cream.
10. A preparation according to any one of claims 7 to 9, **characterized** in that the preparation is a baby care product.
11. A preparation according to any one of claims 7 to 9, **characterized** in that the preparation is an after-shave lotion or a skin tonic.
12. A method of protecting skin from mechanical irritation, **characterized** by applying to the skin a cosmetic preparation containing trimethylglycine as an anhydride or a monohydrate.
13. A method according to claim 12, **characterized** in that the cosmetic preparation contains trimethylglycine in a concentration of 0.1 to

20% by weight, preferably 2 to 10% by weight, particularly 2 to 6% by weight, based on the preparation, in a suitable conventional cosmetic base.

14. A method according to claim 12 or 13, **characterized** in that the cosmetic preparation is a skin care product, a shaving preparation or a
5 depilatory preparation.

15. A method according to any one of claims 12 to 14, **characterized** in that the cosmetic preparation is a foot care product or a hand cream.

16. A method according to any one of claims 12 to 14, **characterized** in that the cosmetic preparation is a baby care product.
10

17. A method according to any one of claims 12 to 14, **characterized** in that the cosmetic preparation is an after-shave lotion or a skin tonic.

Fig. 1B

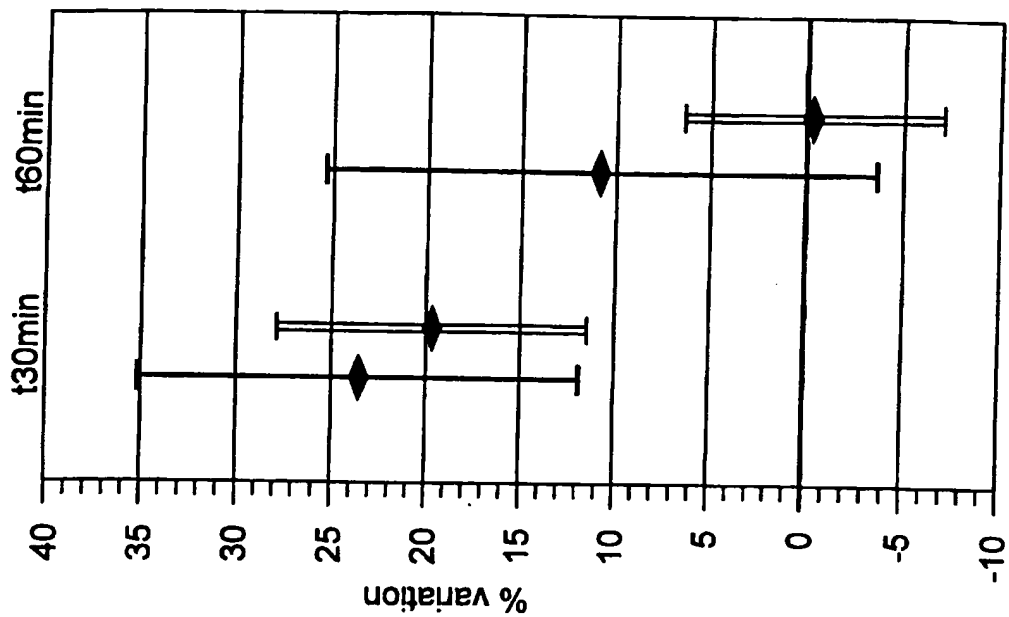
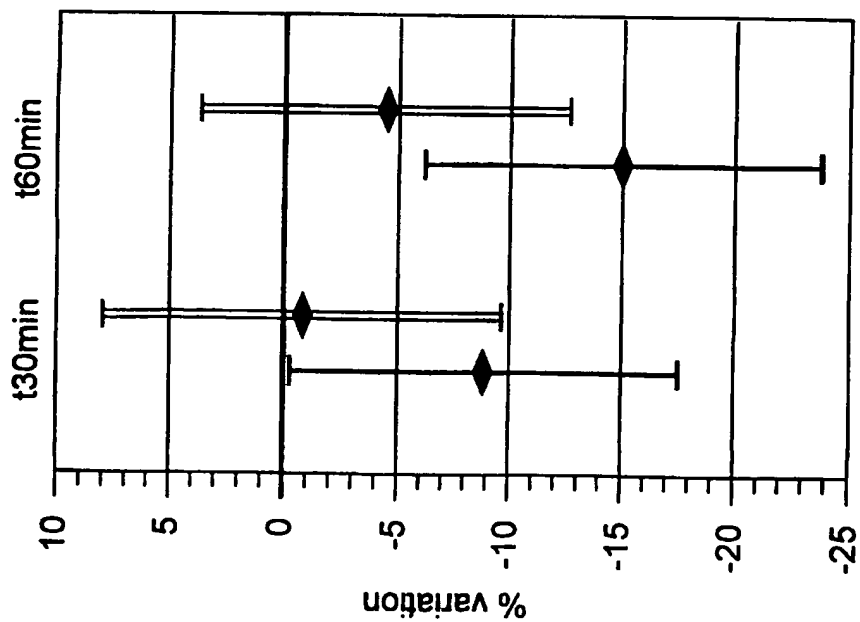


Fig. 1A



= Treated area/
Untreated area 1

= Placebo area/
Untreated area 2

INTERNATIONAL SEARCH REPORT

International application No.

PCT/FI 97/00577

A. CLASSIFICATION OF SUBJECT MATTER

IPC6: A61K 7/48, A61K 7/15, A61K 7/155, A61K 7/50

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC6: A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAPLUS, WPI

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 9118588 A1 (CULTOR LTD.), 12 December 1991 (12.12.91) --	1-17
X	Patent Abstracts of Japan, Vol. 95, No. 11, abstract of JP,A,07309741 (AJINOMOTO CO INC), 28 November 1995 (28.11.95) --	1-17
X	Patent Abstracts of Japan, Vol. 96, No. 3, abstract of JP,A,08081348 (KOBAYASHI PHARMACEUT CO LTD), 26 March 1996 (26.03.96) --	1-17

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"B" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

17 December 1997

Date of mailing of the international search report

09-01-1998

Name and mailing address of the ISA/
Swedish Patent Office
Box 5055, S-102 42 STOCKHOLM
Facsimile No. +46 8 666 02 86

Authorized officer

Gerd Strandell
Telephone No. +46 8 782 25 00

INTERNATIONAL SEARCH REPORT

International application No.

PCT/FI 97/00577

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Patent Abstracts of Japan, Vol. 96, No. 1, abstract of JP,A,08020520 (ASAHI CHEM IND CO LTD), 23 January 1996 (23.01.96) -----	1-17

